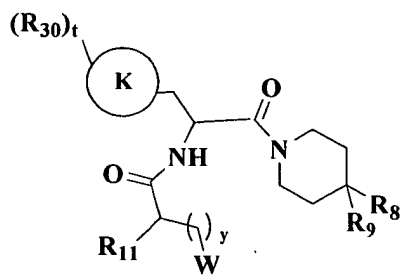
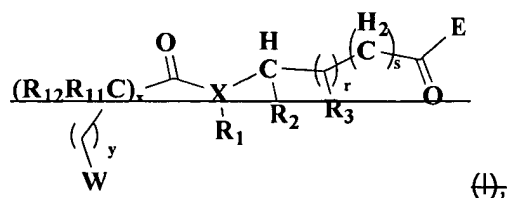


Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

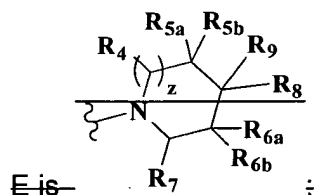
1. (currently amended) A compound according to the formula (I),



or a pharmaceutically-acceptable salt, hydrate or prodrug thereof,

in which

K is aryl or heteroaryl;



X is N or CH;

R₁ is hydrogen or C₁₋₆alkyl or is taken together with R₂ or R₃ to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R₂ is hydrogen, aryl, cycloalkyl, heteroaryl, heterocycle; or C₁₋₆alkyl or C₂₋₆alkenyl optionally substituted with one to three of hydroxy, alkoxy, halogen, cyano, nitro, trifluoromethyl, amino, alkylamino, aryl, cycloalkyl, heteroaryl, and/or heterocycle; or R₂ is taken together with R₁ or R₃ to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R₃ is hydrogen or C₁₋₆alkyl or is taken together with R₁ or R₂ to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R₄, R₅, R_{5a}, R_{5b}, R₆, R_{6a}, R_{6b}, and R₇ are independently selected from hydrogen, alkyl, substituted alkyl, halogen, hydroxy, alkoxy, keto, aryl, heteroaryl, cycloalkyl, and heterocycle, or R_{5a}

and/or ~~R_{5b}, R_{6a} and/or R_{6b}~~ are taken together with R₈ or R₉ to form a fused carbocyclic, heterocyclic or heteroaryl ring;

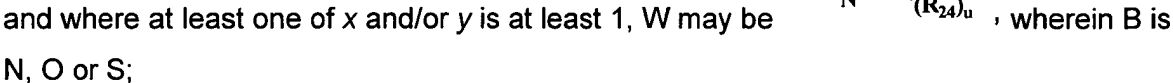
R₈ and R₉ are independently hydrogen, halogen, cyano, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclo, aryl, heteroaryl, -OR₁₃, -NR₁₃R₁₄, -SR₁₃, -S(O)_pR₁₄, -C(=O)R₁₃, -OC(=O)R₁₃, -CO₂R₁₃, -C(=O)NR₁₃R₁₄, -NR₁₃C(=O)R₁₄, -OC(=O)NR₁₃R₁₄, -NR₁₃CO₂R₁₄, -NR₁₃C(=O)NR₁₄R₁₅ or -NR₁₃SO₂R₁₄; or R₈ and R₉ taken together form a monocyclic or bicyclic cycloalkyl or heterocyclo joined in a spiro fashion to the piperidine ring E at C*, provided that R₈ and R₉ are not both hydrogen, and provided further that when R₈ is -OR₁₃, -(CH₂)_k-aryl or -(CH₂)_k-heteroaryl, then R₉ is not -C(=O)NR₁₈R₁₉, -CO₂R₁₉, -(CH₂)_mNR₁₈SO₂R₂₀, -(CH₂)_mNR₁₈C(=O)R₂₀, -(CH₂)_mOR₁₉, -(CH₂)_mO(C=O)R₂₀, -CH(R₁₈)R₁₉, or -(CH₂)_mNR₁₈(C=O)NR₁₉R₂₁;

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R₁₁ and ~~R₁₂~~ are is selected independently of each other from hydrogen, alkyl, halogen, hydroxy, hydroxyalkyl, haloalkyl, amino, aminoalkyl, alkylamino, arylalkyl, cycloalkylalkyl, heteroarylalkyl, aryl, and cycloalkyl, and where y is at least 1, then R₁₁ and ~~R₁₂~~ may be heterocyclo or heterocycloalkyl, or ~~R₁₁ and R₁₂ when attached to the same carbon atom, may join to form a spirocycloalkyl ring;~~

R₁₃, R₁₄ and R₁₅ are independently hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl; or R₁₃ and R₁₄, or R₁₄ and R₁₅ may join together to form a heterocyclo or heteroaryl, except R₁₄ is not hydrogen when joined to a sulfonyl group as in -S(O)_pR₁₄ or -NR₁₃SO₂R₁₄;

W is selected from:

- 1) -NR₁₆R₁₇, -NR₁₆C(=O)R₂₂, -NR₁₆CO₂R₂₂, -OR₂₃, amidino, and guanidino;
- 2) heteroaryl or heterocyclo groups selected from pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, isoxazolyl, thiazolyl, isothiazolyl, 3-azaisothiazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, and pyranyl, wherein said heteroaryl and heterocyclo groups may be substituted or unsubstituted and may have an optionally-substituted carbocyclic, heterocyclic or heteraryl ring fused thereto; or
- 3) a ring selected from:

~~s is 0 or 1;~~

t is 0, 1 or 2;

u and v are 0, 1, 2, or 3;

w is 0, 1, or 2;

~~x~~ and y is are 0, 1, 2, 3, or 4; and

z is 0, 1, or 2.

2. (canceled)

3. (currently amended) A compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof,

in which:

W is $-NR_{16}R_{17}$, $-NHC(=O)R_{22}$, $-NHCO_2\text{alkyl}$, OR_{23} , or azetidiny;

R_{16} and R_{17} are independently selected from hydrogen, $C_{1-8}\text{alkyl}$, and $(CH_2)_q-J$, wherein J is selected from naphthyl, furanyl, indolyl, imidazolyl, pyrimidinyl, benzothienyl, pyridinyl, pyrrolyl, pyrrolidinyl, thienyl, and $C_{3-7}\text{cycloalkyl}$, wherein the alkyl, alkylene, and/or J groups of R_{16} and/or R_{17} are optionally substituted with up to three R_{32} ;

R_{22} is selected from $C_{1-6}\text{alkyl}$, trifluoromethyl, alkoxyalkyl, furylalkyl, alkylaminoethyl, phenyl, pyrrolylalkyl, piperidinyl, and piperidinylalkyl, wherein R_{22} in turn is optionally substituted with one to two $C_{1-4}\text{alkyl}$ and/or $-CO_2(C_{1-4}\text{alkyl})$;

R_{23} is hydrogen or phenyl;

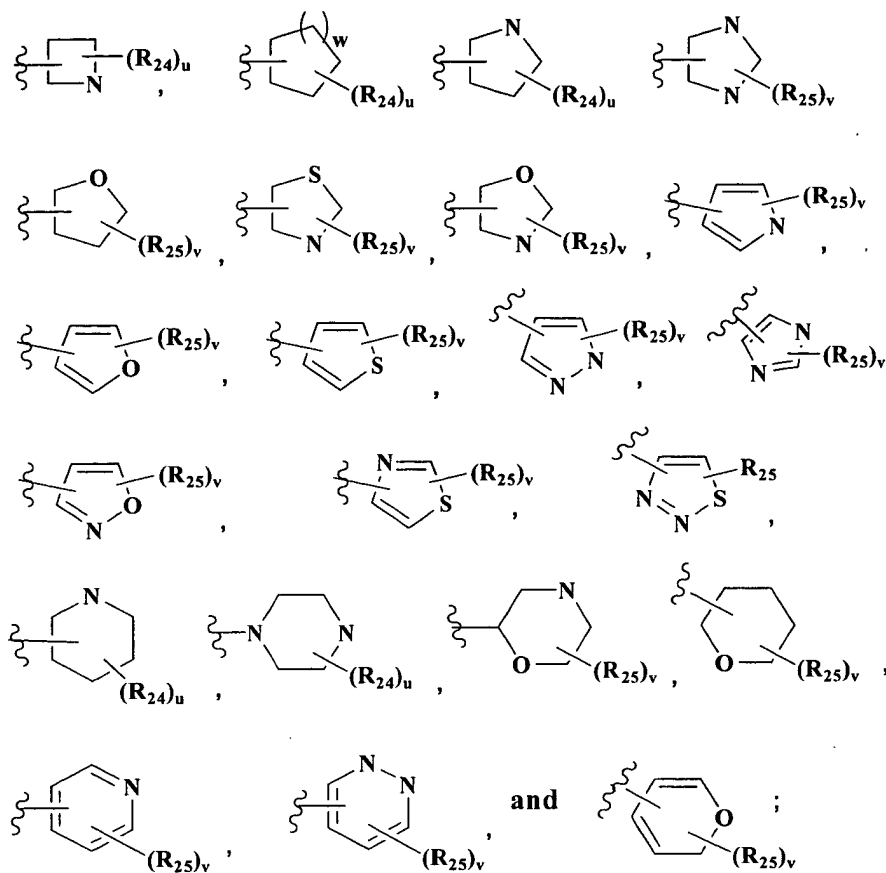
R_{32} is selected from $C_{1-6}\text{alkyl}$, hydroxy, $C_{1-4}\text{alkoxy}$, amino, $C_{1-4}\text{alkylamino}$, amino $C_{1-4}\text{alkyl}$, trifluoromethyl, halogen, phenyl, benzyl, phenyloxy, benzyloxy, $-C(=O)(CH_2)NH_2$, $-CO_2(C_{1-4}\text{alkyl})$, $-SO_2(C_{1-4}\text{alkyl})$, tetrazolyl, piperidinyl, pyridinyl, and indolyl, wherein when R_{32} is a ring, said ring in turn is optionally substituted with one to two $C_{1-4}\text{alkyl}$, hydroxy, methoxy, and/or halogen; and

q is 0, 1, 2 or 3.

4. (currently amended) A compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof,

in which

W is a ring selected from:



and where at least one of x and/or y is at least 1, W may be

S;

R₂₄ is selected from keto (=O), C₁₋₆alkyl, halogen, amino, aminoalkyl, alkylamino, hydroxy, C₁₋

₄alkoxy, hydroxyC₁₋₄alkyl, -C(=O)alkyl, -C(=O)aminoalkyl, -C(=O)phenyl, -C(=O)benzyl, -CO₂alkyl, -CO₂phenyl, -CO₂benzyl, -SO₂alkyl, -SO₂aminoalkyl, -SO₂phenyl, -SO₂benzyl, phenyl, benzyl, phenoxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and each R₂₄ in turn is optionally substituted with one to two R₃₁;

R₂₅ at each occurrence is attached to any available carbon or nitrogen atom of W and is selected

from C₁₋₆alkyl, halogen, amino, aminoalkyl, alkylamino, hydroxy, C₁₋₄alkoxy, hydroxyC₁₋
₄alkyl, -C(=O)alkyl, -C(=O)aminoalkyl, -C(=O)phenyl, -C(=O)benzyl, -CO₂alkyl, -CO₂phenyl, -CO₂benzyl, -SO₂alkyl, -SO₂aminoalkyl, -SO₂phenyl, -SO₂benzyl, phenyl, benzyl, phenoxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and/or two R₂₅ when attached to adjacent carbon atoms may be taken together to form a fused benzo or pyrazolyl ring, and/or two R₂₅ when attached to the same carbon

atom (in the case of a non-aromatic ring) may form keto (=O), and each R_{25} in turn is optionally substituted with up to two R_{31} ;

R_{31} is selected from halogen, trifluoromethyl, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy;

w is selected from 0, 1, or 2; and

u and v are selected from 0, 1, and 2.

5. (currently amended) A compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

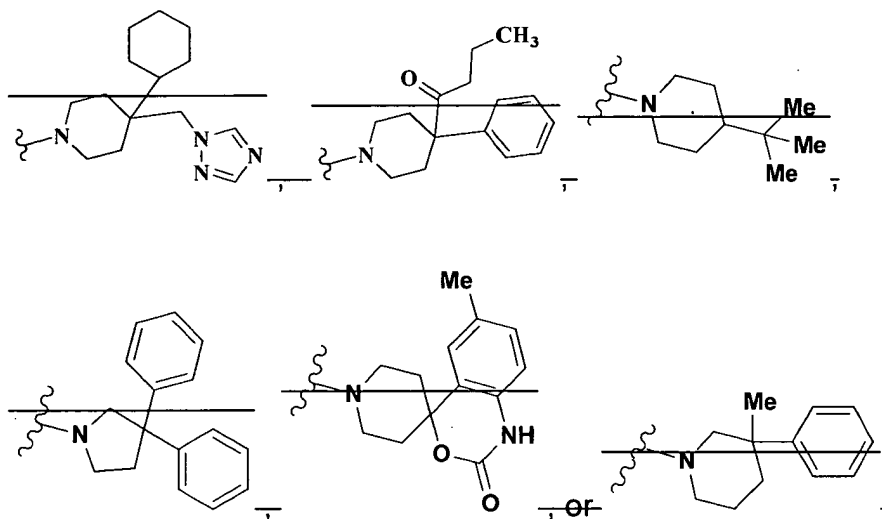
R_8 and R_9 are selected independently from hydrogen, alkyl, $-(CH_2)_j-C(=O)alkyl$, $-(CH_2)_j-phenyl$, $-(CH_2)_j-naphthyl$, $-(CH_2)_j-C_{4-7}cycloalkyl$, $-(CH_2)_j-heterocyclo$, and $-(CH_2)_j-heteroaryl$, or R_8 and R_9 together form a spirocycloalkyl or spiroheterocyclic ring; and

j is selected from 0, 1, 2 and 3.

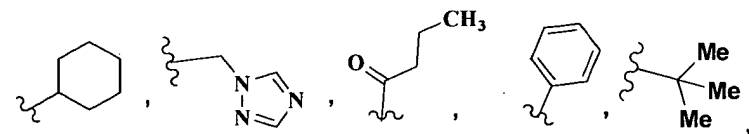
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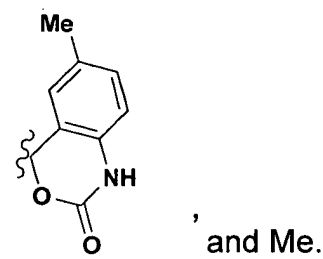
6. (currently amended) A compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

E is



R^8 and R^9 are independently selected from





7. (currently amended) A compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

R_{11} and R_{12} are is (i) at each occasion independently selected from:

- a) hydrogen,
 b) C_{1-6} alkyl,
 c) C_{1-6} alkyl substituted with up to two of hydroxy, alkoxy, amino, alkylamino, imidazolyl, pyrazolyl, phenyl, naphthyl, pyridinyl, indolyl, pyrimidyl, furyl, thiazolyl, and thienyl, wherein said ringed substituents in turn are optionally substituted with one to three R_{33} and/or have a benzene ring fused thereto optionally substituted with one to two R_{33} ;
 d) C_{3-7} cycloalkyl optionally substituted with up to two R_{33} and/or having a benzene ring fused thereto, wherein said fused benzene ring is optionally substituted with up to two R_{33} ;
 e) phenyl optionally substituted with up to three R_{33} ;
 f) where y is at least one, R_{11} and R_{12} may also be selected from piperidinyl, pyrrolidinyl, piperidinylalkyl, and pyrrolidinylalkyl, in turn optionally substituted with up to three R_{33} ; or
 ii) alternatively, one of R_{11} and one of R_{12} attached to the same carbon atom may be taken together to form a spirocycloalkyl ring;

R_{33} is selected from C_{1-6} alkyl, hydroxy, C_{1-6} alkoxy, halogen, nitro, phenyl, benzyl, phenyloxy, benzyloxy, $-C(=O)$ phenyl, amino, alkylamino, and aminoalkyl, wherein when R_{33} includes a phenyl group said phenyl group in turn is optionally substituted with one to two of halogen, nitro, cyano, C_{1-4} alkyl, and/or C_{1-4} alkoxy.

8. (currently amended) A compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

R_2 is selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, biphenyl, C_{2-6} alkenylene-K, and $-(CH_2)_9-K$;

K is selected from phenyl, naphthyl, thienyl, thiazolyl, pyridinyl, pyrimidinyl, and C₅₋₆cycloalkyl, wherein each group K in turn is optionally substituted with one to three R₃₀ or has a benzene ring fused thereto, which also may be substituted with one to three R₃₀;

R₃₀ is selected from C₁₋₄alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and acylphenyl; and

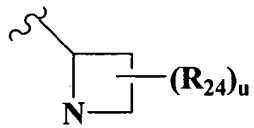
g is 0, 1, 2 or 3.

9. (canceled)

10. (canceled)

11. (currently amended) A compound according to claim 1[0], or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

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W is , -NR₁₆R₁₇, NR₁₆C(=O)R₂₂, OH, or imidazolyl;

R₁₆ and R₁₇ are selected from hydrogen and C₁₋₄alkyl;

R₂₂ is C₁₋₄alkyl, phenyl or piperidinylC₁₋₄alkyl;

R₂₄ is C₁₋₄alkyl; and

u is 0 or 1.

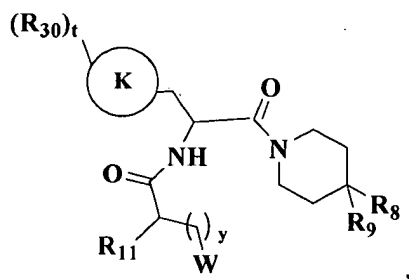
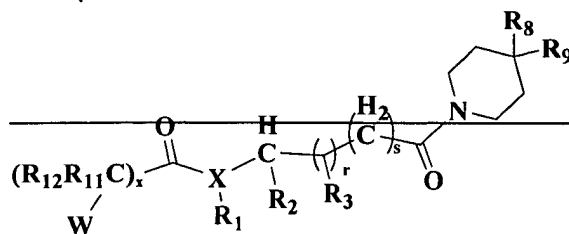
12. (currently amended) A compound according to claim 11, or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

R₁₁ is hydrogen, C₁₋₄alkyl, or imidazolylC₁₋₄alkyl; and

~~R₁₂ is hydrogen or C₁₋₄alkyl.~~

13. (currently amended) A compound according to claim 11, or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which R₁₆ and R₁₇ are independently selected from hydrogen, C₁₋₈alkyl, and C₁₋₈substituted alkyl, except R₁₆ and R₁₇ are not alkyl substituted with pyridinyl, imidazolyl, thiazolyl, pyrimidinyl, or piperazinyl, and W is not morpholinyl.

14. (current amended) A compound according to the formula,



or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which

K is aryl or heteroaryl;

X is N or CH;

R₁ is hydrogen or C₁₋₆ alkyl or is taken together with R₂ or R₃ to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R₂ is hydrogen, aryl, cycloalkyl, heteroaryl, heterocycle; or C₁₋₆ alkyl or C₂₋₆ alkenyl optionally substituted with one to three of hydroxy, alkoxy, halogen, cyano, nitro, trifluoromethyl, amino, alkylamino, aryl, cycloalkyl, heteroaryl, and/or heterocycle; or R₂ is taken together with R₁ or R₃ to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R₃ is hydrogen or C₁₋₆ alkyl or is taken together with R₁ or R₂ to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R₄, R₅, R_{5a}, R_{5b}, R₆, R_{6a}, R_{6b}, and R₇ are independently selected from hydrogen, alkyl, substituted alkyl, halogen, hydroxy, alkoxy, keto, aryl, heteroaryl, cycloalkyl, and heterocycle, or R_{5a} and/or R_{5b}, R_{6a} and/or R_{6b}, are taken together with R₈ or R₉ to form a fused carbocyclic, heterocyclic or heteroaryl ring;

R₈ and R₉ are independently hydrogen, halogen, cyano, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, -OR₁₃, -NR₁₃R₁₄, -SR₁₃, -S(O)_pR₁₄, -C(=O)R₁₃, -OC(=O)R₁₃, -CO₂R₁₃, -C(=O)NR₁₃R₁₄, -NR₁₃C(=O)R₁₄, -OC(=O)NR₁₃R₁₄, -NR₁₃CO₂R₁₄, -NR₁₃C(=O)NR₁₄R₁₅ or -NR₁₃SO₂R₁₄; or R₈ and R₉ taken together form a monocyclic or bicyclic cycloalkyl or heterocycle joined in a spiro fashion to the piperidine ring E at C*;

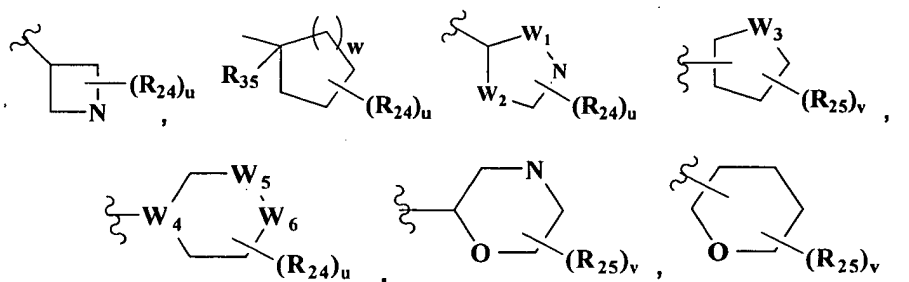
R₁₁ and R₁₂ are is selected independently of each other from hydrogen, alkyl, halogen, hydroxy, hydroxyalkyl, haloalkyl, amino, aminoalkyl, alkylamino, arylalkyl, cycloalkylalkyl, heteroarylalkyl, aryl, and cycloalkyl, and where y is at least 1, then R₁₁ and R₁₂ may be

heterocyclo or heterocycloalkyl, or R_{14} and R_{15} when attached to the same carbon atom, may join to form a spirocycloalkyl ring;

R_{13} , R_{14} and R_{15} are independently hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl; or R_{13} and R_{14} , or R_{14} and R_{15} may join together to form a heterocyclo or heteroaryl, except R_{14} is not hydrogen when joined to a sulfonyl group as in $-S(O)_pR_{14}$ or $-NR_{13}SO_2R_{14}$;

W is selected from:

- 1) $-NR_{16}R_{17}$, $-NR_{16}C(=O)R_{22}$, $-NR_{16}CO_2R_{22}$, or $-OR_{23}$; or
- 2) heteroaryl or heterocyclo groups selected from pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, isoxazolyl, thiazolyl, isothiazolyl, 3-azaisothiazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, and pyranyl, wherein said heteroaryl and heterocyclo groups may be optionally substituted with one to three R_{36} , and may have an optionally-substituted carbocyclic, heterocyclic or heteraryl ring fused thereto; or
- 3) a carbocyclic, heterocyclic, or heteroaryl ring selected from:



in which W_1 and W_2 are NH, CH_2 , O or S, W_3 is O or S, W_4 is N or CH, and W_5 and W_6 are NH or CH_2 , wherein when W_1 , W_2 , W_5 and W_6 are NH or CH_2 , said groups are optionally substituted with R_{24} ;

R_{16} and R_{17} are C_{1-8} alkyl or $(CH_2)_q-J$, wherein J is selected from aryl, heteroaryl, heterocyclo, and cycloalkyl, wherein the alkyl, alkylene, and/or J groups of R_{16} and/or R_{17} are optionally substituted with up to three R_{32} ;

R_{22} is selected from C_{1-6} alkyl, trifluoromethyl, alkoxyalkyl, furylalkyl, alkylaminoethyl, phenyl, pyrrolylalkyl, piperidiny, and piperidinylalkyl, wherein R_{22} in turn is optionally substituted with one to two C_{1-4} alkyl and/or $-CO_2(C_{1-4}alkyl)$;

R_{23} is hydrogen or aryl;

R_{24} and R_{25} at each occurrence are attached to any available carbon or nitrogen atom of W and at each occurrence are selected from hydrogen, C_{1-6} alkyl, halogen, substituted C_{1-6} alkyl, amino, alkylamino, $-C(=O)R_{26}$, $-CO_2R_{26}$, $-SO_2R_{26}$, $-OR_{26}$, aryl, heteroaryl, heterocyclo, and cycloalkyl, and/or two R_{25} attached to two adjacent carbon atoms or adjacent carbon and nitrogen atoms may be taken together to form a fused optionally-substituted heteroaryl,

heterocyclo or cycloalkyl ring, and/or two R_{24} or two R_{25} when attached to the same carbon atom may form keto ($=O$);

R_{26} is hydrogen, alkyl, phenyl, benzyl, or aminoalkyl, except when joined to a sulphonyl group as in SO_2R_{26} , then R_{26} is not hydrogen;;

R_{32} is selected from C_{1-6} alkyl, hydroxy, C_{1-6} alkoxy, halogen, nitro, phenyl, benzyl, phenyloxy, benzyloxy, $-C(=O)$ phenyl, amino, alkylamino, and aminoalkyl, wherein when R_{32} includes a phenyl group said phenyl group in turn is optionally substituted with one to two of halogen, nitro, cyano, C_{1-4} alkyl, and/or C_{1-4} alkoxy;

R_{35} and R_{36} at each occurrence is selected from C_{1-6} alkyl, halogen, substituted C_{1-6} alkyl, hydroxy, alkoxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, acyl, carboxyalkyl, sulfonyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;

p is 1, 2 and 3;

u and v are 0, 1, or 2;

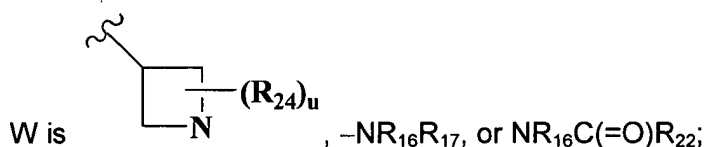
w is 0, 1, or 2; and

~~x is 0, 1, 2, 3, or 4.~~

y is 0, 1, 2, 3, or 4.

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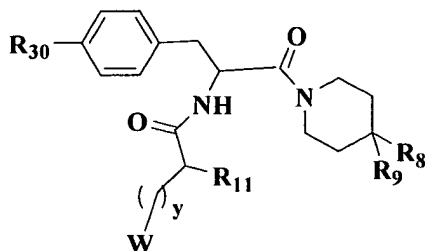
15. (currently amended) A compound according to claim 14, or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, in which



R_{24} is C_{1-4} alkyl;

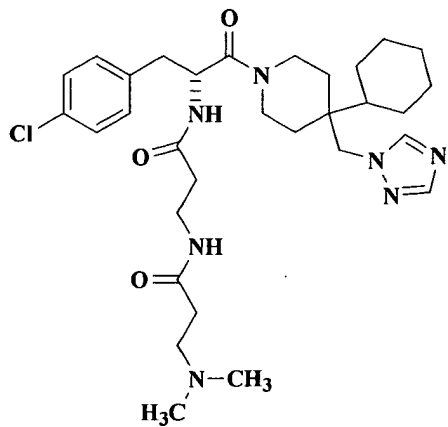
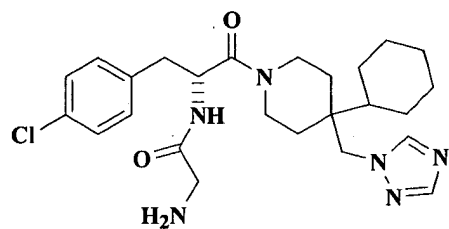
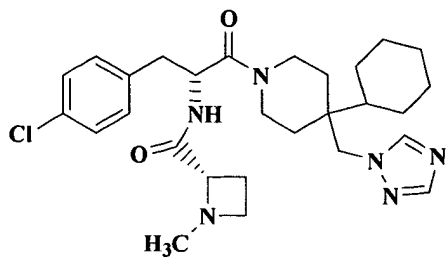
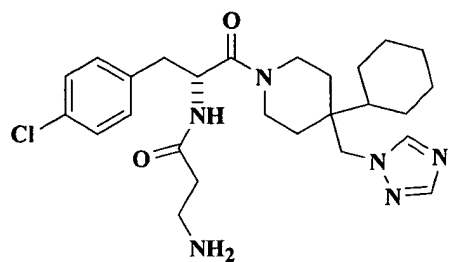
u is 0 or 1.

16. (currently amended) A compound according to claim 14, or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, having the formula,

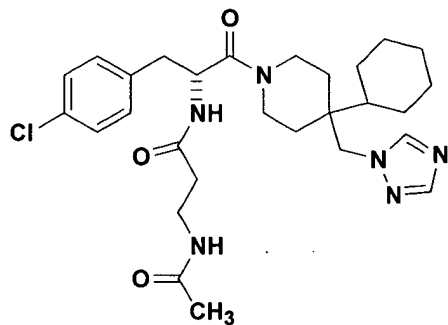
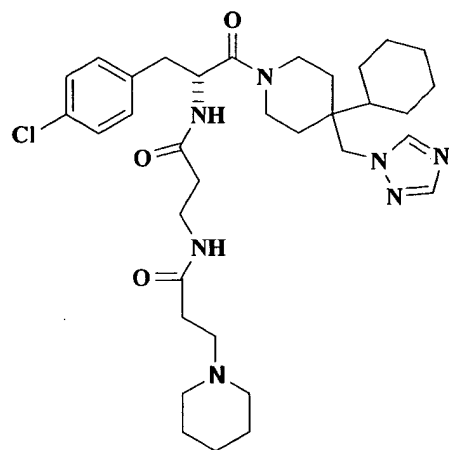


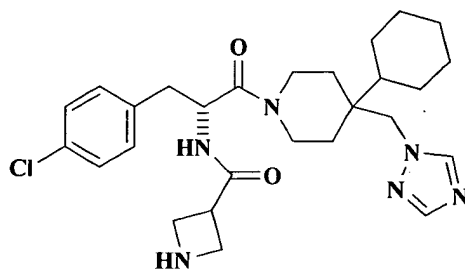
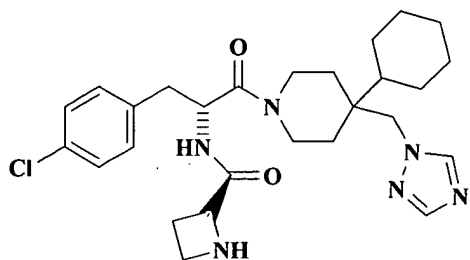
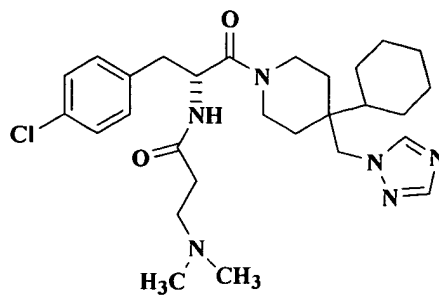
in which $[x']_y$ is 0, 1 or 2 and R_{30} is halogen or methoxy.

17. A compound according to claim 1, having the formula,

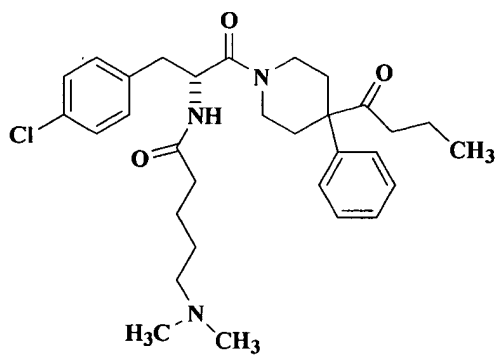
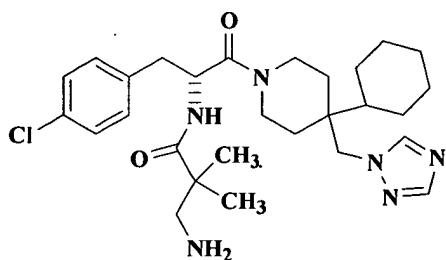
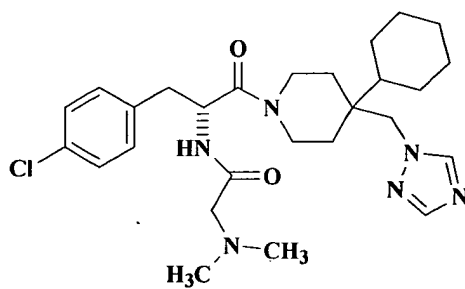
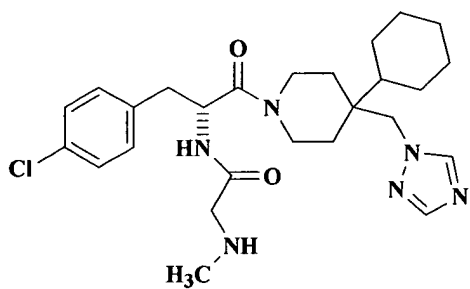


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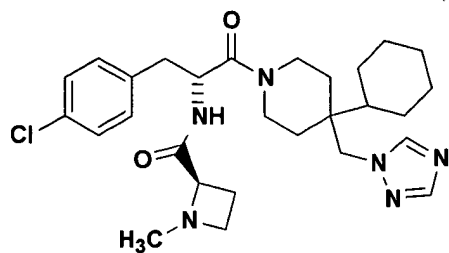




A3



or



or a pharmaceutically-acceptable salt, hydrate or prodrug thereof.

18. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, and a pharmaceutically-acceptable carrier or diluent.

19. A pharmaceutical composition comprising (i) at least one compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, (ii) at least one second compound effective for treating an inflammatory or immune disease, a cardiovascular disease, or neurodegenerative disorder; and (iii) a pharmaceutically-acceptable carrier or diluent.

20. The pharmaceutical composition according to claim 19 in which the at least one second compound comprises a phosphodiesterase inhibitor.

21. A method of treating a melanocortin-receptor associated condition by agonizing melanocortin receptors, the method comprising administering to a warm-blooded species in need of such treatment a therapeutically-effective amount of at least one compound according to claim 1.

22. The method of claim 21 in which the melanocortin-receptor associated condition is an MC-1R or MC-4R associated condition.